AMENDMENTS TO THE SPECIFICATION

Please replace the following paragraphs:

[0097] In one particular embodiment of the present invention, composite promoters utilizing either topoisomerase IIα (topoIIα) and transferrin receptor (TfR) breast cancer-specific control sequences are employed. The topoisomerase IIα (topoIIα) and transferrin receptor (TfR) levels are elevated in breast cancer, as determined using SAGE analysis and cDNA microarray, for example. The present inventors identified a 90 base pair segment (SEQ ID NO:26) and a 116 base pair segment (SEQ ID NO:27) in the 5'-end of topoIIα and TfR promoter, respectively, as a minimally required breast-cancer specific control sequence. In particular embodiments, the promoter activity is enhanced by operatively linking these two short promoters with an enhancer sequence, such as the cytomegalovirus (CMV) promoter enhancer sequence (SEQ ID NO:25); these chimeric promoters are referred to herein as CT90 and CTR116, respectively. The full CT90 promoter is comprised in SEQ ID NO:37, and the full CTR116 promoter is comprised in SEQ ID NO:38. These promoters are described herein but are further characterized in detail in U.S. Provisional Patent Application No. 60/[ ] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein in its entirety. To demonstrate its use in cancer gene therapy, the present inventors generated a DNA construct using CT90 to drive mutant Bik expression. When transfected into cell lines, this construct selectively killed breast cancer cells. Moreover, the present inventors demonstrated that this construct had an anti-tumor effect on breast tumor xenograft in mouse by intravenous injection with an exemplary non-viral delivery system. This indicates that CT90 and CTR116 can drive the expression of a therapeutic gene such as mutant Bik selectively in breast cancer cells.

Please replace the following paragraph:

[0100] The present inventors developed a pancreatic cancer-specific promoter that is described herein but provided in further detail in U.S. Provisional Patent Application 60/[ ] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously

herewith, which is incorporated by reference herein in its entirety. The promoter comprises Cholecystoskinin A receptor (CCKAR) promoter sequence, particularly CCKAR promoter ranging from nt -726 to + 1 (SEQ ID NO:28) operatively linked to an enhancer, such as CMV enhancer. The CCKAR-CMV composite is then engineered with a particular two-step transcriptional amplification (TSTA) system (Iyer et al., 2001; Zhang et al., 2002; Sato et al., 2003; and references cited therein), such as the exemplary GAL4-VP16 or GAL4-VP2 fusion protein, to augment the transcriptional activity and, it is also operatively linked to the post-transcriptional regulatory element of the woodchuck hepatitis virus (WPRE) (SEQ ID NO:29) to modify RNA polyadenylation signal, RNA export, and/or RNA translation. A skilled artisan recognizes that the term "two-step transcriptional amplification (TSTA) system" may also be referred to as "two-step transcriptional activation (TSTA) system" or "recombinant transcriptional activation approach" (Nettelbeck et al., 2000). In a particular aspect, the CCAKAR-TSTA-WPRE (CTP) promoter is utilized, and an example of such a composite promoter is comprised in SEQ ID NO:34. Thus, the molecularly engineered CTP promoter is employed for effective treatment modalities for pancreatic cancer gene therapy with mutant Bik.

Please replace the following paragraph:

[0102] The inventors have developed prostate cancer-specific promoters that may be expected to have benefit for both ADPC and androgen-independent prostate cancer (AIPC) to treat metastatic and recurrent hormonal refractory prostate cancer, particularly to regulate expression of mutant Bik. This promoter is described herein and characterized in further detail in U.S. Provisional Patent Application No. 60/[ ] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein in its entirety. The promoter, referred to herein as ATTP, comprises at least the minimal promoter fragment (hTERTp) of the human telomerase reverse transcriptase (hTERT) (SEQ ID NO:32) operably linked to a two-step transcriptional amplification (TSTA) system, such as the exemplary GAL4-VP16 or GAL4-VP2 (two examples of GAL4-VP2 are SEQ ID NO:30 or SEQ ID NO:33) fusion protein-encoding sequences, and it is also operatively linked to the post-transcriptional regulatory element of the woodchuck hepatitis virus (WPRE) to modify RNA polyadenylation signal, RNA export, and/or RNA translation.

These regulatory sequences are effective in both ADPC and AIPC cell lines. Given that in most cases of recurrent prostate cancers the AR gene is amplified and/or AR is overexpressed, this particular promoter greatly improves the effective index for the embodiment wherein the activity of this system is stimulated by androgen. In preferred embodiments the tissue-specificity region comprises at least, and for example, the ARR2 regulatory element (SEQ ID NO:31) from ARR2 gene. In a particular aspect of the invention, the TSTA-hTERT-ARR2 and WPRE elements are utilized as the prostate cancer-specific regulatory elements, which in specific embodiments are comprised in SEQ ID NO:35. Thus, the present inventors have developed a novel prostate cancer-specific regulatory system that will target mutant Bik to not only ADPC but also AIPC.

Please replace the following paragraph:

[0265] Breast cancer-specific expression of mutant Bik employs two exemplary promoters that are described herein and presented in further detail in U.S. Provisional Patent Application 60/[_____] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein in its entirety.

Please replace the following paragraph:

[0266] A therapeutic construct was generated that comprises topoisomerase IIαcontrol sequence, such as the CT90 region (SEQ ID NO:26), that was operatively linked to CMV enhancer (SEQ ID NO:25), and the composite construct comprising both sequences (SEQ ID NO:37) was operatively linked to a polynucleotide encoding mutant Bik to regulate its expression. The construct is detailed herein but described further in U.S. Provisional Patent Application 60/[_____] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein in its entirety. A particular mutant Bik construct comprising sequence encoding the BikDD mutant is hereinafter referred to as CT90-BikDD. This construct was co-transfected with a luciferase reporter vector into breast cancer cell lines MDA-MB-231 and 468, and the normal breast epithelium cell line 184A1, and then the cell-killing effect was determined by a luciferase vitality assay. The

CMV promoter-driven BikDD vector (CMV-BikDD) and empty vector were used as positive and negative controls, respectively. While CMV-BikDD killed all three cell lines to a nearly equal extent, CT90-BikDD killed breast cancer cells preferentially (FIG. 10), indicating that the killing effect of CT90-BikDD is selective for breast cancer cells. Therefore, CT90 is useful in breast cancer-targeting gene therapy.

Please replace the following paragraph:

[0270] The present inventors also demonstrate in U.S. Provisional Patent Application 60/[ ] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein, that at least part of the transferrin receptor (TR) promoter, such as that comprising SEQ ID NO:27 (CTR116), possesses breast cancer specificity, and in combination with a CMV promoter enhancer (SEQ ID NO:25), for example, it can regulate expression of mutant Bik for effective breast cancer-specific expression. The full CTR116 control sequence (SEQ ID NO:38) comprises SEQ ID NO:25 operatively linked to SEQ ID NO:27.

Please replace the following paragraph:

[0272] The present inventors may utilize pancreatic cancer-specific promoter sequences to control expression of a polynucleotide encoding a mutant Bik polypeptide. One particular but exemplary pancreatic cancer-specific promoter is described herein and is presented in further detail in U.S. Provisional Patent Application 60/[ ] 559,111, entitled "Cancer-Specific Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein in its entirety.

Please replace the following paragraph:

[0276] A prostate cancer-specific promoter sequence is employed to control expression of a polynucleotide encoding a mutant Bik polypeptide. One particular but exemplary pancreatic cancer-specific promoter is described herein and is presented in further detail in U.S. Provisional Patent Application 60/[ ] 559,111, entitled "Cancer-Specific

Promoters" by Mien-Chie Hung, Yan Li, Yong Wen, Chi-Ping Day, Kun-Ming Rau, Xiaoming Xie, Zheng Li, filed simultaneously herewith and incorporated by reference herein in its entirety. In specific embodiments, a prostate cancer-specific promoter that regulates expression of mutant Bik in both androgen-dependent and androgen-independent manners is utilized.